

20000822 144

EEDP-04-26
July 1995



Environmental Effects of Dredging Technical Notes



Methods for the Assessment of the Genotoxic Effects of Environmental Contaminants; Glossary and References

Purpose

This technical note is the third in a series of three that outline and describe the principal methods that have been developed to test the potential of environmental contaminants to cause mutagenic, carcinogenic, and teratogenic effects. The first in this series (EEDP-04-24) describes methods used to discern genotoxic effects at the subcellular level, while the second (EEDP-04-25) describes methods used to discern genotoxic effects at the cellular and organ/organism level.

Recent literature citations for each topic referenced in this series of technical notes are provided in this technical note, in addition to a glossary of terms. The information in these technical notes is intended to provide Corps of Engineers personnel with a working knowledge of the terminology and conceptual basis of genotoxicity testing. To develop an improved understanding of the concepts of genotoxicity, readers are encouraged to review "A Primer in Genotoxicity" (Jarvis, Reilly, and Lutz 1993), presented in Volume D-93-3 of the *Environmental Effects of Dredging* information exchange bulletin.

Additional Information

For additional information, contact the authors, Dr. Michael E. Honeycutt, (601) 634-4300, Ms. A. Susan Jarvis, (601) 634-2804, and Dr. Victor A. McFarland, (601) 634-3721, or the manager of the Environmental Effects of Dredging Programs, Dr. Robert M. Engler, (601) 634-3624.

Glossary

Adduct - a chemically modified macromolecule. An adduct is formed when a compound covalently binds to DNA, hemoglobin, bile, etc.

DISTRIBUTION STATEMENT A

Approved for Public Release
Distribution Unlimited

US Army Engineer Waterways Experiment Station

DTIC QUALITY INSPECTED 4

AGM00-11-3585

Amino acid - an organic acid having the general structure of HO₂C-CHR-NH₂ linked together polymerically to form proteins. The R group determines the specific amino acid. Amino acids are obtained from the diet (essential amino acids) or are synthesized by the body from essential amino acids (non-essential amino acids).

Analog - a compound structurally similar to another.

Antigen-antibody reaction - an antigen is a foreign compound that enters the body. In response to an antigen, particular cells in the body synthesize antibodies, or proteins that bind to the antigen and are highly specific for the antigen. The antigen-antibody complex is recognized by other types of cells in the body, which engulf the antigen-antibody complex for removal from the body. This immune-response principle the body uses to fight infection has been applied to the detection of particular compounds (antigens) of interest. Antibodies to the compound or enzyme of interest are synthesized using biotechnology techniques. The antibodies are labeled with a fluorescent tag that allows visualization using fluorescence techniques.

Autoradiography - a method of visualizing distinct areas of radioactivity in a sample using photographic techniques. Radioactive compounds emit energy in the form of gamma rays or alpha or beta particles, depending on the type of isotope. This energy will expose photographic film in the same manner as visible light, giving a "picture" of the location of radioactivity in a sample.

Bioluminescence - a biochemical reaction occurring in an organism that results in the formation of light energy. An example is the light produced by a firefly.

Biomarker - generally, some biological event that can be used to signal the exposure of an organism to a particular contaminant.

Carcinogen - a compound shown to cause the formation of cancer in an organism.

Cardiac output - blood flow from the heart.

Chromosome - the condensed form of DNA and its associated proteins visible during cell division.

Complementary RNA or DNA (cRNA, cDNA) - a strand of RNA or DNA that is composed of bases complementary to a particular segment of RNA or DNA. RNA is composed of four bases: guanine (G), which is complementary to cytosine (C), and adenine (A), which is complementary to uracil (U). DNA is composed of these same bases, except thymine (T) is substituted for uracil. Complementary bases noncovalently bind (hybridize) with each other. A segment of cDNA for a piece of DNA whose sequence is CCGATAAGT would be GGCTATTCA. cDNA and cRNA are often used as probes.

Conjugation - the covalent bonding of an endogenous molecule to a xenobiotic molecule to facilitate excretion of the xenobiotic.

Covalent bonding - an interaction of two or more separate molecules whereby they become one distinct molecule. For example, two hydrogen and one oxygen atoms may covalently bond to form water.

Cryostatic - techniques that are performed at freezing temperatures.

Cytochrome P450 - a family of enzymes located primarily in the liver that normally function in steroid metabolism, but which also metabolize xenobiotic compounds.

Cytosol - the aqueous portion of a cell and the components dissolved therein. The cytosol is isolated from tissues using ultracentrifugation.

DNA - deoxyribonucleic acid, an extremely long molecule composed of four nucleotides (adenine, thymine, cytosine, guanosine) which contains the genetic makeup of an organism.

Electrophoresis - a method used to separate large electrically charged molecules such as DNA, RNA, or proteins. Electrophoresis uses direct electrical current to cause the charged molecules to migrate through a gel toward the oppositely charged pole of the apparatus.

Endoplasmic reticulum - a flat, membranous, netlike system within the cytoplasm of a cell that, among other functions, contains cytochrome P450.

EROD induction assay - ethoxyresorufin-O-deethylase, or EROD, is a particular cytochrome P450 enzyme that is normally present in the liver in very small quantities, but is induced upon exposure to planar aromatic compounds such as dioxins, furans, and PCBs. For the EROD induction assay, liver hepatoma (cancer) cells grown in culture are dosed with sample extracts and analyzed for EROD activity using a fluorometer. This assay detects picogram (parts per trillion) quantities of 2,3,7,8-TCDD, the most potent EROD inducer, rivaling gas chromatography/mass spectrometry in sensitivity.

Etiologic agent - a compound that can be shown to be the cause for some effect.

Eukaryote - a cell that comprises a multicellular organism. Eukaryotic cells are much more complex than prokaryotic cells, containing more subcellular components.

Fluorescence - the emission of light of a particular wavelength by a compound after absorption of light of another wavelength. Fluorescence is the basis for detection of many compounds and is extremely sensitive and somewhat specific.

Fluorometer - an instrument used to measure fluorescence.

Genome - the DNA of a cell.

Glucose - a simple sugar (monosaccharide) that is utilized by cells for energy.

Glutathione - a tripeptide, γ -glutamylcysteinylglycine, that is found in virtually all species. Glutathione is extremely important in that it helps regulate the reduction-oxidation potential of the cell, acts as an amino acid transport system for the body, and functions in phase II metabolism.

Glycogen - the storage form of glucose. After periods of glucose intake (eating) when blood glucose levels are high, the body stores excess glucose by linking, or polymerizing, the glucose molecules together into a branched chain configuration making glycogen. Glycogen is stored in the liver and muscle.

Hybridize - noncovalent bonding of complementary segments of nucleic acids.

Hyperplasia - an excessive proliferation of normal cells.

Hypertrophy - an enlargement of cellular diameter without accompanying nuclear changes.

Induction - production of a particular protein in response to some stimulus.

Initiation - conversion of a normal cell to a cancerous cell. Initiation is an irreversible change involving the interaction of a carcinogen with DNA, priming the cell for cancer development via promotion.

Lagging - a term used to describe the leaving behind of part of a chromosome during the migration of chromosomes in anaphase during mitosis.

Luminometer - an instrument used to measure bioluminescence.

Macromolecules - large molecules that comprise a cell. Macromolecules include DNA, RNA, and proteins.

Messenger RNA - a strand of RNA that is complementary to a particular segment of DNA (gene) and acts as a template for the translation (production) of a particular protein.

Mutagen - a compound that can cause a mutation, or a change in a specific DNA nucleotide, for example, adduct formation.

Nucleoside - a building block of DNA and RNA. A nucleoside is one of the five nitrogen bases (adenine, guanine, uracil, cytosine, and thymine) linked to a sugar compound called ribose (for RNA) or deoxyribose (for DNA).

Nucleotide - a nucleotide is a nucleoside with a phosphate group attached. Nucleosides must be converted to nucleotides before they can be incorporated into DNA or RNA.

Phase I metabolism - the metabolism of xenobiotic compounds by enzymes which include cytochrome P450. Phase I metabolism usually results in the addition or exposure of a polar functional group, for example, an -OH group, on the xenobiotic. Phase I metabolism readies the xenobiotic for urinary excretion or phase II metabolism.

Phase II metabolism - the metabolism of xenobiotic compounds whereby an endogenous molecule is conjugated with a xenobiotic. Phase II metabolism readies the xenobiotic for biliary excretion.

Probe - a relatively short strand of RNA or DNA that is complementary to a particular gene of interest and is labeled with a fluorescent or radioactive tag. The probe is incubated with isolated DNA or RNA from an organ and hybridizes with the gene of interest. The gene may then be visualized using fluorescent microscopy or autoradiography.

Prokaryote - a bacterial cell. Prokaryotic cells are much simpler than eukaryotic cells, lacking many of the subcellular structures of the eukaryotic cell. One-celled organisms are prokaryotic.

Promotion - the process by which a chemical facilitates the growth and development of initiated cells into a tumor. Promoters do not interact directly with DNA, but generally stimulate an increase in DNA synthesis and/or cell replication in the target cells.

Promutagen - a compound which, when metabolized, is converted into a mutagen.

Teratogen - a compound causing defects in reproduction, resulting either in reduced productivity due to fetal mortality or in the birth of offspring with physical, mental, behavioral, or developmental defects.

Translation - the biosynthesis of amino acids.

Ultracentrifugation - a technique involving centrifugation at extremely high speeds, up to 250,000 times the force of gravity, used to isolate cellular components.

Xenobiotic - a compound foreign to the body. Examples of xenobiotics are pesticides, PAHs, and dioxins.

Selected References

General

1. Al-Sabiti, K. 1991. *Handbook of genotoxic effects and fish chromosomes*, Kristoff, Ljubljana, Republic of Slovenia.
2. Brusick, D. 1989. "Genetic toxicology," *Principles and methods of toxicology*, 2nd ed., A. W. Hayes, ed., Raven, New York, pp 407-434.
3. Hoffman, G. R. 1991. "Genetic toxicology," *Casarett and Doull's toxicology; The basic science of poisons*, 4th ed., M. O. Amdur, J. Doull, and C. D. Klaassen, eds., Pergamon, New York, pp 201-225.
4. Huggett, R. J., Kimerle, R. A., Mehrle, P. M., and Bergman, H. L. 1992. *Biomarkers: Biochemical, physiological and histological markers of anthropogenic stress*, Lewis, Florida.
5. Jarvis, A. S., Reilly, F. J., Jr., and Lutz, C. H. 1993. "A primer in genotoxicity," *Environmental Effects of Dredging*, Vol D-93-3, U.S. Army Engineer Waterways Experiment Station, Vicksburg, MS.
6. Li, A. P., and Heflich, R. H. 1991. *Genetic toxicology*, CRC, Florida.
7. McCarthy, J. F., and Shugart, L. R. 1990. *Biomarkers of environmental contamination*, Lewis, Florida.
8. Singer, B., and Grunberger, D. 1983. *Molecular biology of mutagens and carcinogens*, Plenum, New York.
9. World Health Organization Regional Office for Europe and United Nations Environment Programme. 1990. *Carcinogenic, mutagenic, and teratogenic marine pollutants: Impact on human health and the environment*, Portfolio, Texas.
10. Milman, H. A., and Weisburger, E. K. 1985. *Handbook of carcinogen testing*, Park Ridge, New Jersey.

Ames Assay

11. Ames, B. N., Durston, W. E., Yamasaki, E., and Lee, F. D. 1973. "Carcinogens are mutagens: A simple test system combining liver homogenates for activation and bacteria for detection," *Proceedings, National Academy of Science USA* 70:2281-2285.
12. Ames, B. N., McCann, J., and Yamasaki, E. 1975. "Methods for detecting carcinogens and mutagens with the *Salmonella*/mammalian-microsome mutagenicity test," *Mutation Research* 31:347-364.

13. Bessi, H., Ferard, J. F., Vasseur, P., Colin, F., and Belkadir, E. 1992. "Genotoxicity of hazardous leachates from solid wastes evaluated for environmental impact with the Ames test," *Environmental Toxicology and Water Quality* 7:71-86.
14. Chu, K. C., Patel, K. M., Lin, A. H., Tarone, R. E., Linhart, M. S., and Dunkel, V. C. 1981. "Evaluating statistical analyses and reproducibility of microbial mutagenicity assays," *Mutation Research* 85:119-132.
15. Doerger, J. U., Meier, J. R., Dobbs, R. A., Johnson, R. D., and Ankley, G. T. 1992. "Toxicity reduction evaluation at a municipal wastewater treatment plant using mutagenicity as an endpoint," *Archives of Environmental Contamination and Toxicology* 22:384-388.
16. Durant, J. L., Hemond, H. F., and Thilly, W. G. 1992. "Determination of mutagenicity in sediments of the Aberjona watershed using human lymphoblast and *Salmonella typhimurium* mutation assays," *Environmental Science and Technology* 26:599-608.
17. Dutka, B. J., Kwan, K. K., Rao, S. S., Jurkovic, A., and Liu, D. 1991. "River evaluation using ecotoxicological and microbiological procedures," *Environmental Monitoring and Assessment* 16:287-313.
18. Gatehouse, D. 1987. "Guidelines for testing of environmental agents; Critical features of bacterial mutation assays," *Mutagenesis* 2:397-409.
19. Grifoll, M., Solanas, A. M., and Bayona, J. M. 1990. "Characterization of genotoxic components in sediments by mass spectrometric techniques combined with *Salmonella*/microsome test," *Archives of Environmental Contamination and Toxicology* 19:175-184.
20. Grifoll, M., Solanas, A. M., and Pares, R. 1988. "Assessment of mutagenic activity of coastal sediments off Barcelona," *Toxicity Assessment* 3:315-329.
21. Houk, V. S. 1992. "The genotoxicity of industrial wastes and effluents," *Mutation Research* 277:91-138.
22. Houk, V. S., Goto, S., Endo, O., Claxton, L. D., Lewtas, J., and Matsushita, H. 1992. "Detection of direct-acting mutagens in ambient air: A comparison of two highly sensitive mutagenicity assays," *Environmental Molecular Mutagenesis* 20:19-28.
23. Jones, K. C., and Peace, E. A. 1989. "The Ames mutagenicity assay applied to a range of soils," *Chemosphere* 18:1657-1664.
24. Kinae, N., Hashizume, T., Makita, T., Tomita, I., Kimura, I., and Kanamori, H. 1981. "Studies on the toxicity of pulp and paper mill effluents;

I. Mutagenicity of the sediment samples derived from kraft paper mills." *Water Research* 15:17-24.

25. Kwan, K. K., and Dutka, B. J. 1990. "Simple two-step sediment extraction procedure for use in genotoxicity and toxicity bioassays," *Toxicity Assessment* 5:395-404.

26. Lan, Q., Dickman, M., and Alvarez, M. 1991. "Evidence of genotoxic substances in the Niagara River watershed," *Environmental Toxicology and Water Quality* 6:1-15.

27. Maggard, L. A., Brown, K. W., and Donnelly, K. C. 1987. "The efficiency of two standardized procedures for extracting mutagenic chemicals from soils," *Chemosphere* 16:1243-1255.

28. Maron, D. M., and Ames, B. N. 1983. "Revised methods for the *Salmonella* mutagenicity test," *Mutation Research* 113:173-215.

29. McCann, J., and Ames, B. N. 1976. "Detection of carcinogens as mutagens in the *Salmonella*/microsome test; Assay of 300 chemicals: Discussion," *Proceedings, National Academy of Science USA* 73:950-954.

30. McCann, J., Choi, E., Yamasaki, E., and Ames, B. N. 1975. "Detection of carcinogens as mutagens in the *Salmonella*/microsome test; Assay of 300 chemicals," *Proceedings, National Academy of Science USA* 72:5135-5139.

31. Metcalfe, C. D., Balch, G. C., Cairns, V. W., Fitzsimons, J. D., and Dunn, B. P. 1990. "Carcinogenic and genotoxic activity of extracts from contaminated sediments in western Lake Ontario," *Science of the Total Environment* 94:125-141.

32. West, W. R., Smith, P. A., Booth, G. M., and Lee, M. L. 1988. "Isolation and detection of genotoxic components in a Black River sediment," *Environmental Science and Technology* 22:224-228.

33. West, W. R., Smith, P. A., Booth, G. M., Wise, S. A., and Lee, M. L. 1986. "Determination of genotoxic polycyclic aromatic hydrocarbons in a sediment from the Black River (Ohio)," *Archives of Environmental Contamination and Toxicology* 15:241-249.

Mutatox

34. Dutka, B. J., Kwan, K. K., Rao, S. S., Jurkovic, A., and Liu, D. 1991. "River evaluation using ecotoxicological and microbiological procedures," *Environmental Monitoring and Assessment* 16:287-313.

35. Elmore, E., and Fitzgerald, M. P. 1990. "Evaluation of the bioluminescence assays as screens for genotoxic chemicals," *Mutat. Environ.* 340:379-387.

36. Ho, K. T. Y., and Quinn, J. G. 1993. "Bioassay-directed fractionation of organic contaminants in an estuarine sediment using the new mutagenic bioassay, MutatoxTM," *Environmental Toxicology and Chemistry* 12:823-830.

37. Johnson, B. T. 1992. "Potential genotoxicity of sediments from the Great Lakes," *Environmental Toxicology and Water Quality* 7:373-390.

38. Johnson, B. T. 1992. "An evaluation of a genotoxicity assay with liver S9 for activation and luminescent bacteria for detection," *Environmental Toxicology and Chemistry* 11:473-480.

39. Kwan, K. K., Dutka, B. J., Rao, S. S., and Liu, D. 1990. "Mutatox test: A new test for monitoring environmental genotoxic agents," *Environmental Pollution* 65:323-332.

40. Kwan, K. K., and Dutka, B. J. 1990. "Simple two-step sediment extraction procedure for use in genotoxicity and toxicity bioassays," *Toxicity Assessment* 5:395-404.

41. Ulitzur, S., and Weiser, I. 1981. "Acridine dyes and other DNA-intercalating agents induce the luminescence system of luminous bacteria and their dark variants," *Proceedings, National Academy of Science USA* 78:3338-3342.

42. Ulitzur, S., Weiser, I., and Yannai, S. 1980. "A new, sensitive and simple bioluminescence test for mutagenic compounds," *Mutation Research* 74:113-124.

43. Ulitzur, S. 1986. "Bioluminescence test for genotoxic agents," *Methods in Enzymology* 133:264-274.

44. Weiser, I., Ulitzur, S., and Yannai, S. 1981. "DNA-damaging agents and DNA-synthesis inhibitors induce luminescence in dark variants of luminous bacteria," *Mutation Research* 91:443-450.

³²P-Postlabeling

45. Chipman, J. K., Marsh, J. W., Livingstone, D. R., and Evans, B. 1992. "Genetic toxicity in dab *Limanda limanda* from the North Sea," *Marine Ecology Progress Series* 91:121-126.

46. Jones, N. J., and Parry, J. M. 1992. "The detection of DNA adducts, DNA base changes, and chromosome damage for the assessment of exposure to genotoxic pollutants," *Aquatic Toxicology* 22:323-344.

47. Kurelec, B., Garg, A., Krca, S., and Gupta, R. C. 1989. "DNA adducts as biomarkers in genotoxic risk assessment in the aquatic environment," *Marine Environmental Research* 28:317-321.

48. Kurelec, B., Chacko, M., and Gupta, R. C. 1988. "Postlabeling analysis of carcinogen-DNA adducts in mussel *Mytilus galloprovincialis*," *Marine Environmental Research* 24:317-320.
49. MacCubbin, A. E., Black, J. J., and Dunn, B. P. 1990. "³²P-Postlabeling detection of DNA adducts in fish from chemically contaminated waterways," *Science of the Total Environment* 94:89-104.
50. Nesnow, S., Ross, J., Nelson, G., Holden, K., Erexson, G., Kligerman, A., and Gupta, R. C. 1993. "Quantitative and temporal relationships between DNA adduct formation in target and surrogate tissues: Implications for bio-monitoring," *Environmental Health Perspectives Supplement* 101:37-42.

Alkaline Unwinding Assay

51. Batel, R., Vukmirovic, M., Bihari, N., Zahn, R. K., and Müller, W. E. G. 1993. "Nonradiometric detection of DNA crosslinks in mussel haemolymph by alkaline elution," *Analytical Biochemistry* 212:402-406.
52. Bihari, N., Batel, R., and Zahn, R. 1992. "Fractionation of DNA from marine invertebrate (*Maja crispata*, *Mytilus galloprovincialis*) haemolymph by alkaline elution," *Comparative Biochemistry and Physiology* 102B:419-424.
53. Bradley, M. O., and Dysart, G. 1985. "DNA single-strand breaks, double-strand breaks, and crosslinks in rat testicular germ cells: Measurement of their formations and repair by alkaline and neutral filter elution," *Cell Biology and Toxicology* 1:181-195.
54. Daniel, F. B., Chang, L. W., Schenck, K. M., DeAngelo, A. B., and Skelly, M. F. 1989. "The further development of a mammalian DNA alkaline unwinding bioassay with potential application to hazard identification for contaminants from environmental samples," *Toxicology and Industrial Health* 5:647-665.
55. McCarthy, J. F., Gardner, H., Wolfe, M. J., and Shugart, L. R. 1991. "DNA alterations and enzyme activities in Japanese medaka (*Oryzias latipes*) exposed to diethylnitrosamine," *Neuroscience and Biobehavioral Reviews* 15:99-102.
56. Meyers-Schone, L., Shugart, L. R., Beauchamp, J. J., and Walton, B. T. 1993. "Comparison of two freshwater turtle species as monitors of chemical contamination: DNA damage and residue analysis," *Environmental Toxicology and Chemistry* 13:1487-1496.
57. Nacci, D., and Jackim, E. 1989. "Using the DNA alkaline unwinding assay to detect DNA damage in laboratory and environmentally exposed cells and tissues," *Marine Environmental Research* 28:333-337.
58. Shugart, L. R., McCarthy, J. F., Jimenez, B. D., and Daniel, J. 1987. "Analysis of adduct formation in the bluegill sunfish (*Lepomis macrochirus*)

between benzo[a]pyrene and DNA of the liver and hemoglobin of the erythrocyte," *Aquatic Toxicology* 9:319-327.

59. Shugart, L. R. 1988. "Quantitation of chemically induced damage to DNA of aquatic organisms by alkaline unwinding assay," *Aquatic Toxicology* 13:43-52.

60. Theodorakis, C. W., D'Surley, S. J., and Shugart, L. R. 1994. "Detection of genotoxic insult as DNA strand breaks in fish blood cells by agarose gel electrophoresis," *Environmental Toxicology and Chemistry* 13:1023-1032.

61. Theodorakis, C. W., D'Surley, S. J., Bickham, J. W., Lyne, T. B., Bradley, B. P., Hawkins, W. E., Farkas, W. L., McCarthy, J. F., and Shugart, L. R. 1992. "Sequential expression of biomarkers in bluegill sunfish exposed to contaminated sediment," *Ecotoxicology* 1:45-73.

Unscheduled DNA Synthesis

62. Droy, B. F., Miller, M. R., Freeland, T. M., and Hinton, D. E. 1988. "Immunohistochemical detection of CCl_4 -induced, mitosis-related DNA synthesis in livers of trout and rat," *Aquatic Toxicology* 13:155-166.

63. West, W. R., Smith, P. A., Booth, G. M., Wise, S. A., and Lee, M. L. 1986. "Determination of genotoxic polycyclic aromatic hydrocarbons in a sediment from the Black River (Ohio)," *Archives of Environmental Contamination and Toxicology* 15:241-249.

64. West, W. R., Smith, P. A., Booth, G. M., and Lee, M. L. 1986. "Determination and genotoxicity of nitrogen heterocycles in a sediment from the Black River," *Environmental Toxicology and Chemistry* 5:511-519.

65. West, W. R., Smith, P. A., Booth, G. M., and Lee, M. L. 1988. "Isolation and determination of genotoxic components in a Black River sediment," *Environmental Science and Technology* 22:224-228.

Cytochrome P450

66. Elskus, A. A., Stegeman, J. J., Susani, L. C., Black, D., Pruell, R. J., and Fluck, S. J. 1989. "Polychlorinated biphenyls concentration and cytochrome P450E expression in winter flounder from contaminated environments," *Marine Environmental Research* 28:25-30.

67. Gallagher, E. P., and Di Giulio, R. T. 1989. "Effects of complex waste mixtures on hepatic monooxygenase activities in brown bullheads (*Ictalurus nebulosus*)," *Environmental Pollution* 62:113-128.

68. Hektoen, H., Bernhoft, A., Ingebrigtsen, K., Skaare, J. U., and Goksøyr, A. 1994. "Response of hepatic xenobiotic metabolizing enzymes in rainbow

trout (*Oncorhynchus mykiss*) and cod (*Gadus morhua*) to 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD)," *Aquatic Toxicology* 28:97-106.

69. Holm, G., Norrgren, L., Andersson, T., and Thuren, A. 1993. "Effects of exposure to food contaminated with PBDE, PCN, or PCB on reproduction, liver morphology and cytochrome P450 activity in the three-spined stickleback, *Gasterosteus aculeatus*," *Aquatic Toxicology* 27:33-50.

70. Lorenzen, A., and Okey, A. B. 1990. "Detection and characterization of [³H]2,3,7,8-tetrachlorodibenzo-p-dioxin binding to Ah receptor in a rainbow trout hepatoma cell line," *Toxicology and Applied Pharmacology* 106:53-62.

71. Masfaraud, J. F., Monod, G., and Devaux, A. 1990. "Use of fish cytochrome P450-dependent 7-ethylresorufin o-deethylase activity as a biochemical indicator of water pollution; Study of the liver and the kidney of male and female nase (*Chondrostoma nasus*) from the river Rhône," *Science of the Total Environment* 97/98:729-738.

72. Nasci, C., Campesan, G., Fossato, V. U., Tallandini, L., and Turchetto, M. 1991. "Induction of cytochrome P450 and mixed function oxygenase activity by low concentrations of polychlorinated biphenyls in marine fish *Zosterisessor ophiocephalus* (Pall.)," *Aquatic Toxicology* 19:281-290.

73. Payne, J. F., Fancey, L., Kiceniuk, J., Williams, U., Osborne, J., and Rahimtula, A. 1985. "Mixed-function oxygenases as biological monitors around petroleum hydrocarbon development sites: Potential for induction by diesel and other drilling mud base oils containing reduced levels of polycyclic aromatic hydrocarbons," *Marine Environmental Research* 17:328-332.

74. Pesonen, M., Goksøyr, A., and Andersson, T. 1992. "Expression of P4501A1 in a primary culture of rainbow trout hepatocytes exposed to β-naphthoflavone or 2,3,7,8-tetrachlorodibenzo-p-dioxin," *Archives of Biochemistry and Biophysics* 292:228-233.

75. Rice, D. W., Seltenrich, C. P., Keller, M. L., Spies, R. B., and Felton, J. S. 1994. "Mixed-function oxidase-specific activity in wild and caged speckled sanddabs *Citharichthys stigmaeus* in Elkhorn Slough, Moss Landing Harbor and nearshore Monterey Bay, California," *Environmental Pollution* 84:179-188.

76. Sawyer, T., Bandiera, S., and Safe, S. 1983. "Bioanalysis of polychlorinated dibenzofuran and dibenzo-p-dioxin mixtures in fly ash," *Chemosphere* 12:529-535.

77. Stegeman, J. J., Teng, F. Y., and Snowberger, E. A. 1987. "Induced cytochrome P450 in winter flounder (*Pseudopleuronectes americanus*) from coastal Massachusetts evaluated by catalytic assay and monoclonal antibody probes," *Canadian Journal of Fisheries and Aquatic Science* 4:1270-1277.

78. Stegeman, J. J., Woodin, B. R., Park, S. S., Kloepffer-Sams, P. J., and Gelboin, H. V. 1985. "Microsomal cytochrome P450 function in fish evaluated with polyclonal and monoclonal antibodies to cytochrome P450E from scup (*Stenotomus chrysops*)," *Marine Environmental Research* 17:83-86.

79. Sulaiman, N., George, S., and Burke, M.D. 1991. "Assessment of sublethal pollutant impact on flounders in an industrialised estuary using hepatic biochemical indices," *Marine Ecology Progress Series* 68:207-212.

80. Tillitt, D. E., and Giesy, J. P. 1991. "Characterization of the H4IIE rat hepatoma cell bioassay as a tool for assessing toxic potency of planar halogenated hydrocarbons in environmental samples," *Environ. Sci. Technol.* 25:87-92.

81. van der Weiden, M. E. J., Tibosch, H. J. H., Bleumink, R., Sinnige, T. L., van de Guchte, C., Seinen, W., and van den Berg, M. 1993. "Cytochrome P450 1A induction in the common carp (*Cyprinus carpio*) following exposure to contaminated sediments with halogenated polyaromatics," *Chemosphere* 27: 1297-1309.

Bile Metabolites

82. Ariese, F., Kok, S. J., Verkaik, M., Gooijer, C., Velhorst, N. H., and Hofstraat, J. W. 1993. "Synchronous fluorescence spectrometry of fish bile: A rapid screening method for the biomonitoring of PAH exposure," *Aquatic Toxicology* 26:273-286.

83. Di Giulio, R. T., Habig, C., and Gallagher, E. P. 1993. "Effects of Black Rock Harbor sediments on indices of biotransformation, oxidative stress, and DNA integrity in channel catfish," *Aquatic Toxicology* 26:1-22.

84. Krahn, M. M., Burrows, D. G., MacLeod, W. D., Jr., and Malins, D. C. 1987. "Determination of individual metabolites of aromatic compounds in hydrolyzed bile of English sole (*Parophrys vetulus*) from polluted sites in Puget Sound, Washington," *Archives of Environmental Contamination and Toxicology* 16:511-522.

85. Wachtmeister, C. A., Förlin, L., Arnoldsson, K. C., and Larsson, J. 1991. "Fish bile as a tool for monitoring aquatic pollutants: Studies with radioactively labeled 4,5,6-trichloroguaiacol," *Chemosphere* 22:39-46.

Phase II Enzymes

86. Ankley, G. T., Blazer, V. S., Reinert, R. E., and Agosin, M. 1986. "Effects of aroclor 1254 on cytochrome P-450-dependent monooxygenase, glutathione S-transferase, and UDP-glucuronosyltransferase activities in channel catfish liver," *Aquatic Toxicology* 9:91-103.

87. Hao, X., Castro, V. M., Bergh, J., Sundström, B., and Mannervik, B. 1994. "Isoenzyme-specific quantitative immunoassays for cytosolic glutathione

transferases and measurement of the enzymes in blood plasma from cancer patients and in tumor cell lines," *Biochimica et Biophysica Acta* 1225:223-230.

88. Hida, T., Kuwabara, M., Ariyoshi, Y., Takahashi, T., Sugiura, T., Hosoda, K., Niitsu, Y., and Ueda, R. 1994. "Serum glutathione S-transferase- π level as a tumor marker for non-small cell lung cancer," *Cancer* 73:1377-1382.

89. Kamata, T., Akasaka, K., Ohrui, H., and Meguro, H. 1994. "Fluorometric assay of glutathione peroxidase activity in liver and plasma with N-(9-acridinyl)maleimide," *Bioscience, Biotechnology, and Biochemistry* 58:878-880.

90. Prochaska, H. J., and Fernandes, C. L. 1993. "Elevation of serum phase II enzymes by anticarcinogenic enzyme inducers: Markers for a chemo-protected state?" *Carcinogenesis* 14:2441-2445.

Heat Shock Proteins

91. Bols, N. C., Mosser, D. D., and Steels, G. B. 1992. "Temperature studies and recent advances with fish cells in vitro," *Comparative Biochemistry and Physiology* 103A:1-14.

92. Bond, J., Gonzalez, C. R. M., and Bradley, B. P. 1993. "Age-dependent expression of proteins in the cladoceran *Daphnia magna* under normal and heat-stress conditions," *Comparative Biochemistry and Physiology* 106B:913-917.

93. Perdew, G. W., and Whitelaw, M. L. 1991. "Evidence that the 90-kDa heat shock protein (HSP90) exists in cytosol in heteromeric complexes containing HSP70 and three other proteins with M_r of 63,000, 56,000, and 50,000," *Journal of Biological Chemistry* 266:6708-6713.

Cytotoxicity

94. Babich, H., Rosenberg, D. W., and Borenfreund, E. 1991. "In vitro cytotoxicity studies with the fish hepatoma cell line, PLHC-1 (*Poeciliopsis lucida*)," *Ecotox. Environ. Safety* 21:327-336.

95. Babich, H., and Borenfreund, E. 1991. "Cytotoxicity and genotoxicity assays with cultured fish cells: A review." *Toxicology In Vitro* 1:91-100.

96. Brandão, J. C., Bohets, H. H. L., Van De Vyver, I. E., and Dierickx, P. J. 1992. "Correlation between the in vitro cytotoxicity to cultured fathead minnow fish cells and fish lethality data for 50 chemicals," *Chemosphere* 25:553-562.

97. Calleja, M. C., Persoone, G., and Geladi, P. 1994. "Comparative acute toxicity of the first 50 multicentre evaluation of in vitro cytotoxicity chemicals to aquatic non-vertebrates," *Archives of Environmental Contamination and Toxicology* 26:69-78.

98. Dierickx, P. J. 1993. "Comparison between fish lethality data and the in vitro cytotoxicity of lipophilic solvents to cultured fish cells in a two-compartment model," *Chemosphere* 27:1511-1518.
99. Ryan, J. A., and Hightower, L. E. 1994. "Evaluation of heavy-metal ion toxicity in fish cells using a combined stress protein and cytotoxicity assay," *Environmental Toxicology and Chemistry* 13:1231-1240.
100. Vega, M. M., Castaño, A., Blazquez, T., and Tarazona, J. V. 1994. "Assessing organic toxic pollutants in fish-canning factory effluents using cultured fish cells," *Ecotoxicology* 3:79-88.

Ornithine Decarboxylase

101. Bisschop, A., van Rooijen, L. A. A., Derkx, H. J. G. M., and van Wijk, R. 1981. "Induction of rat hepatic ornithine decarboxylase by the tumor promoters 12-O-tetradecanoylphorbol-13-acetate and phenobarbital in vivo; Effect of retinyl-acetate," *Carcinogenesis* 2:1283-1287.
102. Heby, O. 1981. "Role of polyamines in the control of cell proliferation and differentiation," *Differentiation* 19:1-20.
103. Koza, R. A., Moore, M. J., and Stegeman, J. J. 1992. "Elevated ornithine decarboxylase activity in winter flounder exhibiting cellular lesions," *Marine Environmental Research* 34:19-23.
104. Nebert, D. W., Jensen, N. M., Perry, J. W., and Oka, T. 1980. "Association between ornithine decarboxylase induction and the *Ah* locus in mice treated with polycyclic aromatic compounds," *Journal of Biological Chemistry* 255:6836-6842.
105. O'Brien, T. G., and Diamond, L. 1977. "Ornithine decarboxylase induction and DNA synthesis in hamster embryo cell cultures treated with tumor-promoting phorbol diesters," *Cancer Research* 37:3895-3900.
106. Olson, J. W., and Russell, D. H. 1980. "Prolonged ornithine decarboxylase induction in regenerating carcinogen-treated liver," *Cancer Research* 40: 4373-4380.
107. Osborne, H. B., Cormier, P., Lorillon, O., Maniey, D., and Belle, R. 1993. "An appraisal of the developmental importance of polyamine changes in early *Xenopus* embryos," *International Journal of Developmental Biology* 37:615-618.
108. Pegg, A. E. 1988. "Polyamine metabolism and its importance in neoplastic growth and as a target for chemotherapy," *Cancer Research* 48:759-774.
109. Tome, M. E., Fiser, S. M., and Gerner, E. W. 1994. "Consequences of aberrant ornithine decarboxylase regulation in rat hepatoma cells," *Journal of Cellular Physiology* 158:237-244.

Oxidative Stress

110. Abukhalaf, I. K., Covington, S., Zimmerman, E. G., Dickson, K. L., Masaracchia, R. A., and Donahue, M. J. 1994. "Purification of the 70-kDa heat-shock protein from catfish liver: Immunological comparison of the protein in different fish species and its potential use as a stress indicator," *Environmental Toxicology and Chemistry* 13:1251-1257.
111. Babich, H., Palace, M. R., and Stern, A. 1993. "Oxidative stress in fish cells: In vitro studies." *Archives of Environmental Contamination and Toxicology* 24:173-178.
112. Lemaire, P., Matthews, A., Förlin, L, and Livingstone, D. R. 1994. "Stimulation of oxyradical production of hepatic microsomes of flounder (*Platichthys flesus*) and perch (*Perca fluviatilis*) by model and pollutant xenobiotics," *Archives of Environmental Contamination and Toxicology* 26:191-200.
113. Malins, D. C. 1993. "Identification of hydroxyl radical-induced lesions in DNA base structure: Biomarkers with a putative link to cancer development," *Journal of Toxicology and Environmental Health* 40:247-261.
114. Nagele, A., Felix, K., and Lengfelder, E. 1994. "Induction of oxidative stress and protection against hydrogen peroxide-mediated cytotoxicity by the superoxide dismutase-mimetic complex copper-putrescine-pyridine," *Biochemical Pharmacology* 47:555-562.
115. Pinamonti, S., Chicca, M. C., Muzzoli, M., Papi, A., Fabbri, L. M., and Ciaccia, A. 1994. "Oxygen radical scavengers inhibit clastogenic activity induced by sonication of human serum," *Free Radical Biology and Medicine* 16:363-371.
116. Thomas, P., and Wofford, H. W. 1993. "Effects of cadmium and aroclor 1254 on lipid peroxidation, glutathione peroxidase activity, and selected antioxidants in Atlantic croaker tissues," *Aquatic Toxicology* 27:159-178.
117. Yim, M. B., Chae, H. Z., Rhee, S. G., Chock, P. B., and Stadtman, E. R. 1994. "On the protective mechanism of the thiol-specific antioxidant enzyme against the oxidative damage of biomacromolecules," *Journal of Biological Chemistry* 269:1621-1626.
118. Yu, B. P. 1994. "Cellular defenses against damage from reactive oxygen species," *Physiological Reviews* 74:139-162.

Micronucleus Assays

119. Brunetti, R., Fumagalli, O., Valerio, P., and Gabriele, M. 1992. "Genotoxic effects of anoxia on *Mytilus galloprovincialis*," *Marine Ecology Progress Series* 83:71-74.

120. Brunetti, R., Gabriele, M., Valerio, P., and Fumagalli, O. 1992. "The micronucleus test: Temporal pattern of baseline frequency in *Mytilus galloprovincialis*," *Marine Ecology Progress Series* 83:75-78.
121. Brunetti, R., Majone, F., Gola, I., and Beltrame, C. 1988. "The micronucleus test: Examples of application to marine ecology," *Marine Ecology Progress Series* 44:65-68.
122. Das, R. K., and Roy, B. 1988. "A simplified method for micronucleus preparation from hepatic cells," *Stain Technology* 63(2):71-74.
123. De Flora, S., Vigano, L., D'Agostini, F. D., Camoirano, A., Bagnasco, M., Bennicelli, C., Melodia, F., and Arillo, A. 1993. "Multiple genotoxicity biomarkers in fish exposed in situ to polluted river water," *Mutation Research* 319:167-177.
124. Gabriele, M., Brunetti, R., and Majone, F. 1992. "The micronucleus test in cultured mammalian cells and in *Mytilus* gill tissue," *APLY* 20:103-107.
125. Gauthier, L., Van der Gaag, M. A., L'Haridon, J., Ferrier, V., and Fernanadez, M. 1993. "In vivo detection of waste water and industrial effluent genotoxicity: Use of the newt micronucleus test (Jaylet test)," *Science of the Total Environment* 138:249-269.
126. Hose, J. E., Cross, J. N., Smith, S. G., and Diehl, D. 1987. "Elevated circulating erythrocyte micronuclei in fishes from contaminated sites off southern California," *Marine Environmental Research* 22:167-176.
127. Krauter, P. W. 1993. "Micronucleus incidence and hematological effects in bullfrog tadpoles (*Rana catesbeiana*) exposed to 2-acetylaminofluorene and 2-aminofluorene," *Archives of Environmental Contamination and Toxicology* 24:487-493.
128. Metcalfe, C. D. 1988. "Induction of micronuclei and nuclear abnormalities in the erythrocytes mudminnows (*Umbra limi*) and brown bullheads (*Ictalurus nebulosus*)," *Bulletin of Environmental Contamination and Toxicology* 40:489-495.
129. Panda, K. K., Lenka, M., and Panda, B. B. 1990. "Monitoring and assessment of mercury pollution in the vicinity of a chloralkali plant; I. Distribution, availability, and genotoxicity of sediment mercury in the Rushikulya estuary, India," *Science of the Total Environment* 96:281-296.
130. Seelbach, A., Fissler, B., and Madle, S. 1993. "Further evaluation of a modified micronucleus assay with V79 cells for detection of aneugenic effects," *Mutation Research* 303:163-169.
131. Vanparys, P., Deknudt, G., Germeiren, F., Sysamns, M., and Marsboom, R. 1992. "Sampling times in micronucleus testing," *Mutation Research* 282: 191-196.

132. Williams, R. C., and Metcalfe, C. D. 1992. "Development of an in vivo hepatic micronucleus assay with rainbow trout," *Aquatic Toxicology* 23:193-202.

Sister Chromatid Exchanges

133. Dixon, D. R., Jones, I. M., and Harrison, F. L. 1985. "Cytogenetic evidence of inducible processes linked with metabolism of a xenobiotic chemical in adult and larval *Mytilus edulis*," *Science of the Total Environment* 46:1-8.

134. Eckl, P. M., Anderson-Carnahan, L., and Jirtle, R. L. 1993. "Aquatic genotoxicity testing with rat hepatocytes in primary culture; I. SCE induction," *Science of the Total Environment* 136:111-119.

135. Kelsey, K. T., Xia, F., Bodell, W. J., Spengler, J. D., Christiani, D. C., Dockery, D. W., and Liber, H. L. 1994. "Genotoxicity to human cells induced by air particulates isolated during the Kuwait oil fires," *Environmental Research* 64:18-25.

136. Leung, H. W. 1994. "Evaluation of the genotoxic potential of alkylene-amines," *Mutation Research* 320:31-43.

137. Ohe, T., Ito, H., and Kawabuti, M. 1993. "Genotoxicity of blue rayon extracts from river waters using sister chromatid exchange in cultured mammalian cells," *Archives of Environmental Contamination and Toxicology* 25:293-297.

138. Perry, P., and Wolff, S. 1974. "New Giesma method for the differential staining of sister chromatids," *Nature* 251:156-158.

139. Perry, P., and Evans, H. J. 1975. "Cytological detection of mutagen-carcinogen exposure by sister chromatid exchange," *Nature* 258:121-125.

140. Pesch, G. G. 1990. "Sister chromatid exchange and genotoxicity measurements using polychaete worms," *Review of Aquatic Science* 2:19-25.

141. Pesch, G. G., Mueller, C., Pesch, C. E., Heltshe, J., and Shauer, P. S. 1985. "Application of sister chromatid exchange in marine polychaetes to Black Rock Harbor sediment; Laboratory documentation phase," Technical Report D-85-1, U.S. Army Engineer Waterways Experiment Station, Vicksburg, MS.

142. van der Hoeven, J. C. M., Bruggeman, I. M., Alink, G. M., and Koeman, J. H. 1982. "The killifish *Nothobranchius rachowi*, a new animal in genetic toxicology," *Mutation Research* 97:35-42.

143. Van der Gaag, M. A., and Van de Kerkhoff, J. F. J. 1985. "Mutagenicity testing of water with fish: A step forward to a reliable assay," *Science of the Total Environment* 47:293-298.

Chromosome Aberrations

144. Adler, I. D., and Parry, J. M. 1993. "Development of screening tests for aneuploidy induction by environmental pollutants," *Environmental Health Perspectives Supplement* 101:5-9.
145. Al-Sabiti, K. 1986. "Clastogenic effects of five carcinogenic-mutagenic chemicals on the cells of the common carp, *Cyprinus carpio* L.," *Comparative Biochemistry and Physiology* 85C(1):5-9.
146. Al-Sabiti, K. 1985. "Frequency of chromosomal aberrations in the rainbow trout, *Salmo gairdneri* Rich., exposed to five pollutants," *Journal of Fish Biology* 26:13-19.
147. Anderson, S. L., Hose, J. E., and Knezovich, J. P. 1994. "Genotoxic and developmental effects in sea urchins are sensitive indicators of effects of genotoxic chemicals," *Environmental Toxicology and Chemistry* 13:1033-1041.
148. Baksi, S. M., and Means, J. C. 1988. "Preparation of chromosomes from early stages of fish for cytogenetic analysis," *Journal of Fish Biology* 32: 321-325.
149. Kocan, R. M., Powell, D. B., and Ligouri, V. M. 1985. "Relationship between visible and heritable chromosome damage in trout cells and embryos," *Marine Environmental Research* 17:320-323.
150. Means, J. C., Daniels, C. B., and Baksi, S. M. 1988. "Development of in vivo genotoxicity tests in estuarine fish and their application to aquatic toxicology," *Marine Environmental Research* 24:327-331.
151. Natarajan, A. T., Darroudi, F., Mullenders, L. H. F., and Meijers, M. 1986. "The nature and repair of DNA lesions that lead to chromosomal aberrations induced by ionizing radiation," *Mutation Research* 160:231-236.
152. Perry, D. M., Weis, J. S., and Weis, P. 1988. "Cytogenetic effects of methylmercury in embryos of the killifish, *Fundulus heteroclitus*," *Archives of Environmental Contamination and Toxicology* 17:569-574.
153. Prein, A. E., Thie, G. M., Alink, G. M., and Koeman, J. H. 1978. "Cytogenetic changes in fish exposed to water of the River Rhine," *Science of the Total Environment* 9:287-291.
154. Renner, H. W., and Wever, J. 1988. "Comparison of the mutagenic response in small intestine epithelium and in bone marrow of Chin. hamsters by chemical mutagens," *Chemosphere* 17:1885-1890.
155. Yager, J. W., and Wiencke, J. K. 1993. "Enhancement of chromosomal damage by arsenic: Implications for mechanism," *Environmental Health Perspectives Supplement* 101:79-82.

Histopathology

156. Bauman, P. C., Harshbarger, J. C., and Hartman, K. J. 1990. "Relationship between liver tumors and age in brown bullhead populations from two Lake Erie tributaries," *Science of the Total Environment* 94:71-87.
157. Becker, D. S., Ginn, T. C., Landolt, M. L., and Powell, D. B. 1987. "Hepatic lesions in English sole (*Parophrys vetulus*) from Commencement Bay, Washington (USA)," *Marine Environmental Research* 23:153-173.
158. Black, J. J. 1988. "Carcinogenicity tests with rainbow trout embryos: A review," *Aquatic Toxicology* 11:129-142.
159. Carr, R. S., Hillman, R. E., and Neff, J. M. 1991. "Field assessment of biomarkers for winter flounder," *Marine Pollution Bulletin* 22:61-67.
160. Couch, J. A., and Harshbarger, J. C. 1985. "Effects of carcinogenic agents on aquatic animals: An environmental and experimental overview," *Environmental Carcinogenesis Reviews* 3:63-105.
161. Gardner, G. R., and Yevich, P. P. 1988. "Comparative histopathological effects of chemically contaminated sediment on marine organisms," *Marine Environmental Research* 24:311-316.
162. Harshbarger, J. C., and Clark, J. B. 1990. "Epizootiology of neoplasms in bony fish of North America," *Science of the Total Environment* 94:1-32.
163. Hawkins, W. E., Overstreet, R. M., and Walker, W. W. 1988. "Carcinogenicity tests with small fish species," *Aquatic Toxicology* 11:113-128.
164. Hawkins, W. E., Walker, W. W., Overstreet, R. M., Lytle, J. S., and Lytle, T. F. 1990. "Carcinogenic effects of some polycyclic aromatic hydrocarbons on the Japanese medaka and guppy in waterborne exposures," *Science of the Total Environment* 94:155-167.
165. Hayes, M. A., Smith, I. R., Rushmore, T. H., Crane, T. L., Thorn, C., Kocal, T. E., and Ferguson, H. W. 1990. "Pathogenesis of skin and liver neoplasms in white suckers from industrially polluted areas in Lake Ontario," *Science of the Total Environment* 94:105-123.
166. Hinton, D. E., Lantz, R. C., Hampton, J. A., McCuskey, P. R., and McCuskey, R. S. 1987. "Normal versus abnormal structure: Considerations in morphologic responses of teleosts to pollutants," *Environmental Health Perspectives* 71:139-146.
167. James, M. O., Hawkins, W. E., and Walker, W. W. 1994. "Phase 1 and phase 2 biotransformation and carcinogenicity of 2-acetylaminofluorene in medaka and guppy," *Aquatic Toxicology* 28:79-94.

168. Johnson, L. L., Stehr, C. M., Olson, O. P., Myers, M. S., Pierce, S. M., Wigren, C. A., McCain, B. B., and Varanasi, U. 1993. "Chemical contaminants and hepatic lesions in winter flounder (*Pleuronectes americanus*) from the northeast coast of the United States," *Environmental Science and Technology* 27: 2759-2771.

169. Khan, R. A., Barker, D. E., Hooper, R., Lee, E. M., Ryan, K., and Nag, K. 1994. "Histopathology in winter flounder (*Pleuronectes americanus*) living adjacent to a pulp and paper mill," *Archives of Environmental Contamination and Toxicology* 26:95-102.

170. Kinae, N., Yamashita, M., Tomita, I., Kimura, I., Ishida, H., Kumai, H., and Nakamura, G. 1990. "A possible correlation between environmental chemicals and pigment cell neoplasia in fish," *Science of the Total Environment* 94:143-153.

171. Köhler, A. 1989. "Regeneration of contaminant-induced liver lesions in flounder—experimental studies toward the identification of cause-effect relationships," *Aquatic Toxicology* 14:203-232.

172. Köhler, A. 1990. "Identification of contaminant-induced cellular and subcellular lesions in the liver of flounder (*Platichthys flesus* L.) caught at differently polluted estuaries," *Aquatic Toxicology* 16:271-294.

173. Malins, D. C., McCain, B. B., Landahl, J. T., Myers, M. S., Krahn, M. M., Brown, D. W., Chan, S. L., and Roubal, W. T. 1988. "Neoplastic and other diseases in fish in relation to toxic chemicals: An overview," *Aquatic Toxicology* 11:43-67.

174. Mix, M. C. 1986. "Cancerous diseases in aquatic animals and their association with environmental pollutants: A critical literature review," *Marine Environmental Research* 20:1-141.

175. Myers, M. S., Olson, O. P., Johnson, L. L., Stehr, C. S., Hom, T., and Varanasi, U. 1992. "Hepatic lesions other than neoplasms in subadult flatfish from Puget Sound, Washington: Relationships with indices of contaminant exposure," *Marine Environmental Research* 34:45-51.

176. Myers, M. S., Landahl, J. T., Krahn, M. M., Johnson, L. L., and McCain, B. B. 1990. "Overview of studies on liver carcinogenesis in English sole from Puget Sound: Evidence for a xenobiotic chemical etiology; I. Pathology and epizootiology," *Science of the Total Environment* 94:33-50.

177. Overstreet, R. M. 1988. "Aquatic pollution problems, southeastern U.S. coasts: Histopathological indicators," *Aquatic Toxicology* 11:213-239.

178. Stein, J., Reichert, W. L., Nishimoto, M., and Varanasi, U. 1990. "Overview of studies on liver carcinogenesis in English sole from Puget Sound:

Evidence for a xenobiotic chemical etiology; II. Biochemical studies," *Science of the Total Environment* 94:51-69.

179. Wester, P. W., and Canton, J. H. 1986. "Histopathological study of *Oryzias latipes* (medaka) after long-term β -hexachlorocyclohexane exposure," *Aquatic Toxicology* 9:21-45.

Developmental Abnormalities

180. Anderson, S. L., Hose, J. E., and Knezovich, J. P. 1994. "Genotoxic and developmental effects in sea urchins are sensitive indicators of effects of genotoxic chemicals," *Environmental Toxicology and Chemistry* 13:1033-1041.

181. Bantle, J. A., Fort, D. J., and Dawson, D. A. 1988. "Bridging the gap from short-term teratogenesis assays to human health hazard assessment by understanding common modes of teratogenic action," *Aquatic Toxicology and Hazard Assessment*, Vol 12, ASTM 1027, U. M. Cowgill and L. R. Williams, eds., American Society for Testing and Materials, PA, pp 46-58.

182. Bantle, J. A., Fort, D. J., and James, B. L. 1989. "Identification of developmental toxicants using the Frog Embryo Teratogenesis Assay-*Xenopus* (FETAX)," *Hydrobiologia* 188/189:577-585.

183. Biegel, L., Howie, L., and Safe, S. 1989. "Polychlorinated biphenyl (PCB) congeners as 2,3,7,8-TCDD antagonists: Teratogenicity studies," *Chemosphere* 19:955-958.

184. Cameron, P., and Berg, J. 1992. "Morphological and chromosomal aberrations during embryologic development in dab *Limanda limanda*," *Marine Ecology Progress Series* 91:163-169.

185. Daniels, C. B., and Means, J. C. 1989. "Assessment of the genotoxicity of produced water discharges associated with oil and gas production using a fish embryo and larval test," *Marine Environmental Research* 28:303-307.

186. Dawson, D. A., Stebler, E. F., Burks, S. L., Bantle, J. A. 1988. "Evaluation of the developmental toxicity of metal-contaminated sediments using short-term fathead minnow and frog embryo-larval assays," *Environmental Toxicology and Chemistry* 7:27-34.

187. Fent, K., and Meier, W. 1994. "Effects of triphenyltin on fish early life stages," *Archives of Environmental Contamination and Toxicology* 27:224-231.

188. Harrison, F. L., Knezovich, J. P., and Rice, D. W. 1984. "The toxicity of copper to the adult and early life stages of the freshwater clam, *Corbicula manilensis*," *Archives of Environmental Contamination and Toxicology* 13:85-92.

189. Jackim, E., and Nacci, D. 1986. "Improved sea urchin DNA-based embryo growth toxicity test," *Environmental Toxicology and Chemistry* 5:561-565.

190. Kocan, R. M., von Westernhagen, H., Landolt, M. L., and Furstenberg, G. 1987. "Toxicity of sea-surface microlayer: Effects of hexane extract on Baltic herring (*Clupea harengus*) and Atlantic cod (*Gadus morhua*) embryos," *Marine Environmental Research* 23:291-305.

191. Laughlin, R. B., Jr., Gustafson, R. G., and Pendoley, P. 1989. "Acute toxicity of tributyltin (TBT) to early life history stages of the hard shell clam, *Mercenaria mercenaria*," *Bulletin of Environmental Contamination and Toxicology* 42:352-358.

192. Linder, G., Barbitta, J., and Kwaiser, T. 1990. "Short-term amphibian toxicity tests and paraquat toxicity assessment," *Aquatic Toxicology and Risk Assessment*, Vol 13, ASTM STP 1096, W. G. Landis and W. H. van der Schalie, eds., American Society for Testing and Materials, Philadelphia, PA, pp 189-198.

193. Longwell, A. C., Chang, S., Hebert, A., Hughes, J. B., and Perry, D. 1992. "Pollution and developmental abnormalities of Atlantic fishes," *Environmental Biology of Fishes* 35:1-21.

194. McKenney, C. L., Jr., and Costlow, J. D., Jr. 1982. "The effects of mercury on developing larvae of *Rhithropanopeus harrisii* (Gould)," *Estuarine, Coastal, and Shelf Science* 14:193-213.

195. Pegano, G., Anselmi, B., Dinnel, P. A., Esposito, A., Guida, M., Iaccarino, M., Melluso, G., Pascale, M., and Trieff, N. M. 1993. "Effects on sea urchin fertilization and embryogenesis of water and sediment from two rivers in Campania, Italy," *Archives of Environmental Contamination and Toxicology* 25: 20-26.

196. Scudder, B. C., Carter, J. L., and Leland, H. V. 1988. "Effects of copper on development of fathead minnow, *Pimephales promelas* Rafinesque," *Aquatic Toxicology* 12:107-124.

197. Shirazi, M. A., and Dawson, D. A. 1991. "Developmental malformation of frog embryos: An analysis of teratogenicity of chemical mixtures," *Archives of Environmental Contamination and Toxicology* 21:177-182.

198. Singer, M. M., George, S., Jacobson, S., Lee, I., Tjeerdema, R. S., and Sowby, M. L. 1994. "Comparative toxicity of Corexit® 7664 to the early life stages of four marine species," *Archives of Environmental Contamination and Toxicology* 27:130-136.

199. Weis, J. S., and Weis, P. 1989. "Effects of environmental pollutants on early fish development," *Aquatic Science* 1:45-73.

200. Weis, J. S., and Kim, K. 1988. "Tributyltin is a teratogen in producing deformities in limbs of the fiddler crab, *Uca pugilator*," *Archives of Environmental Contamination and Toxicology* 17:583-587.

201. Weis, J. S., and Weis, P. 1987. "Pollutants as developmental toxicants in aquatic organisms," *Environmental Health Perspectives* 71:77-85.

INTERNET DOCUMENT INFORMATION FORM

A . Report Title: METHODS FOR THE ASSESSMENT OF THE GENOTOXIC EFFECTS OF ENVIRONMENTAL CONTAMINANTS; GLOSSARY AND REFERENCES

B. DATE Report Downloaded From the Internet: 08/15/00

C. Report's Point of Contact: (Name, Organization, Address, Office Symbol, & Ph #): US Army Engineer Waterways Experiment Station Environmental Laboratory
PO Box 631
Vicksburg, Mississippi 39181-0631

D. Currently Applicable Classification Level: Unclassified

E. Distribution Statement A: Approved for Public Release

F. The foregoing information was compiled and provided by:
DTIC-OCA, Initials: LF Preparation Date 08/21/00

The foregoing information should exactly correspond to the Title, Report Number, and the Date on the accompanying report document. If there are mismatches, or other questions, contact the above OCA Representative for resolution.